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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/245,549	02/05/99	ZERVOS A	10287/039001

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EXAMINER	
TUNG, J	
ART UNIT	**PAPER NUMBER**
1656	7

DATE MAILED: 02/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/245,549	Zervos
Examiner	**Group Art Unit**
Joyce Tung	1653

☒ Responsive to communication(s) filed on *Dec 2, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-31* is/are pending in the application.

Of the above, claim(s) *28-31* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Notice to comply

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1653.

1. Claims 28-31 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected Group II and III. Election of Group I, claims 1-27 was made **without** traverse in Paper No. 6.

Sequence Rules

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

APPLICANT IS GIVEN THE RESPONSE PERIOD SET FORTH IN THIS OFFICE ACTION WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR 1.821-1.825. Failure to comply with these requirements will result in **ABANDONMENT** of the application under 37 CFR 1.821(g).

Information Disclosure Statement

3. The reference AP lined through was not considered because International Search Report is not a publication.

Claim Rejections - 35 U.S.C. § 112

4. Claims 2 and 3-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 2 and 3-27 are vague and indefinite because it is unclear whether the language "said first primers having a first region homologous with the first common sequence of the nucleic acid molecule" means that the first region of the said first primers is complementary to the first common sequence of the nucleic acid molecule. Does this indicate that the first region of the said first primers hybridizes to the first common sequence of the nucleic acid molecule for amplification. It is also unclear whether the language "said second primers having a first region homologous with the second common sequence of the nucleic acid molecule" Does this indicate that the first region of the said second primers hybridizes to the second common sequence of the nucleic acid molecule for amplification. It is suggested to clarify uncertainty. In the examination process, the language is interpreted as a regular primer pair which is used in a conventional polymerase chain reaction for amplification of a target nucleic acid sequence.

b. Claim 22 is vague and indefinite because of the language "is derived from". It is unclear what is the metes and bounds of the said mRNA from a cancerous tissue since the language "derived from" is for making derivatives which might be chemically modified. It is suggested to clarify uncertainty.

Claim Rejections - 35 U.S.C. § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-4, 6-12, 15-22, 25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jorgensen (5,925,544).

Jorgensen discloses a homologous recombination method to amplify in vivo a DNA sequence B present in a genome of a parent cell comprising integrating in a genome of the cell a DNA construct C-M-A-D (See the Abstract). Both A and C denote a DNA sequence is homologous with a genomic DNA fragment either flanking or overlapping a DNA sequence B and the sequence C is located in the opposite end the sequence B. D denotes a DNA sequence is homologous with a genomic DNA fragment located distal for C as compared to B. (See the Abstract). The DNA sequence is at least 8 consecutive base pair in length or may be longer, e.g. thousands nucleotides (See column 3, lines 40-44). A cDNA of genomic library may be prepared

from the organism (See column 7, lines 49-51). This suggests that cDNA may be from plasmid or phage or mRNA or cancerous tissue which are organism. The DNA sequence B is amplified by inverse PCR (See column 7, lines 49-62 and column 8, lines 3-19). The host cell can be a bacterial or fungal (including yeast) cell (See column 6, lines 29-33). Based upon the disclosure of Jorgensen, the DNA sequence A, C and D are not identical. The vector is linearized between the first and second regions of the vector (See column 8, fig. 2, lines 58-64). cDNA is screened when an expression product is known for an activity of the product and thereby identify a clone from which the activity is expressed (See column 7, lines 62-67).

Jorgensen does not disclose gap repair involved in the method. However, the method is a homologous recombination which inherits gap repair. This was well known in the art at the time of the instant invention. Jorgensen also does not disclose using a plurality of host cells, nucleic acid molecule and first and second primers, but Jorgensen indicates that a genomic library may be prepared. This suggests that a plurality of host cell and nucleic acid molecule are used for preparing a DNA library and a plurality of primers are used for the amplification of a desired DNA sequence. Additionally, Jorgensen dose not disclose a kit for practicing the method.

The teachings of Jorgensen suggest the limitations of instant claims 1-4, 6-12, 15-22, 25 and 27. Instant claims 1-4, 6-12, 15-22, 25 and 27 are drawn to a method and kit for constructing a DNA library *in vivo* comprising providing a plurality of host cells, a vector, introducing a vector and a nucleic acid insert molecule into each of the host cells and the method is homologous recombination. The method also involves preparing a plurality of nucleic acid insert molecules

comprising providing a plurality of a first and second primers and a reaction mixture for amplifying the nucleic acid insert molecules. The host cell is a yeast cell or bacterial cell. The vector is linearized between the first and second regions of the vector.

One or ordinary skill in the art at the time of the instant invention would have been motivated to apply the reference of Jorgensen to construct a DNA library because Jorgensen suggest that a cDNA library may prepared (See column 7, lines 40-62) and the method has obtained an increased number of genomically integrated copies of the DNA sequence desired (See the Abstract). An artisan of ordinary skill in the art at the time of the instant invention would have made the kit as claimed including all ingredients which are used for practicing the method because it was routine practice in the art at the time of the instant invention. It would have been prima facie obvious to carry out the method as claimed.

7. Claims 3 and 13 -14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jorgensen (5,925,544) in view of Fraser et al. (4,870,023).

Instant claim 3 is rejected under 35 U.S.C. 103(a) over Jorgensen via the teachings set forth in section 6 above.

Jorgensen does not disclose using a adapter to ligate the nucleic acid insert molecule in which the adapter has a sequence homologous to the first and second region of the vector respectively.

Fraser et al. disclose the invention directed to recombination of baculoviruses which encode fusion polyhedrin protein (See the Abstract). The gene can be expressed via homologous

recombination in vivo with a parent vector (See column 9, lines 25-30). The method involves using a linker which ligates the polyhedrin DNA into a cloning vector (See column 17, lines 9-14). The linker of Fraser et al. has the same function as the adapter claimed in instant claims 13-14.

The teachings of Jorgensen and Fraser et al. suggest the limitations of the instant claims 3 and 13-14. The description of instant claim 3 is set forth in section 6 above. Instant claims 13 and 14 recite further limitations to instant claim 3 in which an adapter is used to ligate the nucleic acid insert molecule to the vector.

One of ordinary skill in the art at the time of the instant invention would have been motivated to combine the references of Jorgensen and Fraser et al. for a reasonable expectation of success because Jorgensen suggest that a cDNA library may prepared (See column 7, lines 40-62) and the method has obtained an increased number of genomically integrated copies of the DNA sequence desired (See the Abstract) and the method of Fraser et al. is useful for express vector (See column 3, lines 2-5). It would have been prima facies obvious to make the adapter as claimed.

8. Claims 3, 23-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jorgensen (5,925,544) in view of Liu et al. (5,928,868).

Instant claim 3 is rejected under 35 U.S.C. 103(a) over Jorgesen via the teachings set forth in section 6 above.

Jorgensen does not disclose that the DNA library is screened in a two hybrid system.

Liu et al. disclose a method and kit for characterizing small molecules from a small molecule library (See the Abstract). The cells respectively contains a first and second expression vector including a DNA encoding a known first and second target linked to a first and second transcriptional module selected from a DNA binding protein and a transcriptional activator (See column 14, lines 9-67). The cells contains a reporter gene. The expression of the reporter gene is conditioned on the proximity of the first and second hybrid proteins to each other, if the hybrid ligand binds to target sites on both hybrid protein. The cells express the reporter gene which are selected (See the Abstract). The method is rapid to identify a small molecule (See column 2, lines 25-30).

The teachings of Jorgensen and Liu et al. suggest the limitations of instant claims 23-24 and 26. Instant claims 23-24 recite further limitations to claim 3 in which DNA library is screened in a two-hybrid system and the vector includes a transcriptional factor activation domain, the host cells has nucleic acid molecule encoding a hybrid protein comprising a transcription factor DNA-binding domain and a detectable gene. The cells are plated onto selective media. Instant claim 26 is drawn to a method of constructing a DNA library for screening in a two-hybrid system comprising constructing the DNA library and introducing the components for making the two-hybrid screening system in a host cell.

One of ordinary skill in the art would have been motivated to combine the references of Jorgensen and Liu et al. for a reasonable expectation of success because the method of Jorgensen has obtained an increased number of genomically integrated copies of the DNA sequence desired

(See the Abstract) and Jorgensen suggests cDNA may be prepared from the organism (See column 7, lines 49-51) and the method of Liu et al. is rapid to a small molecule (See column 2, lines 25-30). It would have been prima facie obvious to carry out the method as claimed.

9. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached at (703) 308-1152.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1653 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

February 11, 2000

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600
2/14/2000